**AJINOMOTO CORPORATE SERVICES LLC**
1120 Connecticut Avenue, N.W., Suite 1010, Washington, D.C. 20036-3953, U.S.A.
Tel: (202) 457-0284 Fax: (202) 457-0107

September 29, 2004

Division of Dockets Management
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

**Re: Comments on FDA Docket No. 2004N-0081: Use of Materials Derived From Cattle in Human Food and Cosmetics**

To Whom It May Concern:

Ajinomoto Corporate Services, LLC, wishes to comment on the interim final rule entitled "Use of Materials Derived From Cattle in Human Food and Cosmetics," Docket No. 2004N-0081 (RIN–0910–AF47). We respectfully submit that this rule could be strengthened and provide additional protection of the food supply and the public health from bovine spongiform encephalopathy (BSE) and related transmissible spongiform encephalopathies (TSEs). We believe this could be accomplished by prohibiting the use of bovine blood-derived products, such as beef blood plasma and fibrinogen, which have a high risk potential for transmitting TSEs to humans. Unless and until bovine blood-derived products are demonstrated to not have the potential for transmitting TSEs to humans, we believe it is critical to public health to prohibit these products from the food supply.

## A. Background

On January 26, 2004, the Department of Health and Human Services announced new safeguards designed to strengthen the existing regulatory structure for preventing the transmission of BSE in the U.S. As part of this initiative, on July 14, 2004, the Food and Drug Administration (FDA) promulgated the above-referenced interim final rule in an effort to protect the food and cosmetics supply from bovine-derived materials that may carry a risk of transmitting BSE. Prohibited bovine-derived material include specified risk material, small intestine

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of all cattle, material from nonambulatory disabled cattle, material from cattle not inspected and passed for human consumption, and mechanically separated beef. Specified risk materials are defined as the brain, skull, eyes, trigeminal ganglia, spinal cord, the majority of the vertebral column, and dorsal root ganglia of cattle 30 months and older, and the tonsils and distal ileum of the small intestine of all cattle.

### B. Prohibited Material

The list of prohibited bovine-derived material was compiled in an attempt by FDA and the U.S. Department of Agriculture (USDA) to "...minimize human exposure to materials that scientific studies have demonstrated are highly likely to contain the BSE agent in cattle infected with the disease." 1/ Nevertheless, as stated in the preamble to the above-referenced interim final rule, "[t]he pathogenisis of TSEs is poorly understood," 2/ as is the transmission of TSEs between species. While the exact route of exposure between cattle products contaminated with the agent that causes BSE and BSE's human counterpart, variant Creutzfeldt-Jakob disease (vCJD), is not fully elucidated, the consensus among scientists is that vCJD is caused by consumption of bovine-derived products contaminated with the BSE agent. 3/

The most prevalent theory in the scientific community regarding the transmission of TSE from cattle to humans is that the agent is a prion, an abnormal form of a normal prion protein that is primarily expressed in neurons. 4/ Studies in cattle have demonstrated that the BSE agent infects a variety of nervous tissue, including the brain, spinal cord and dorsal root ganglia. The distal ileum of the gastrointestinal tract has been found to be infected, as well, which is not surprising based on the theory that consumption of contaminated products is central to the transmission of the disease. Based on the fact that "[d]ata on the distribution of

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1/ 69 Fed. Reg. 42256 (July 14, 2004).

2/ *Id.* at 42257.

3/ *See id.*

4/ *See id.*

BSE infectivity in tissues are incomplete," 5/ however, we believe that FDA's scope of prohibited bovine-derived material is too narrow.

The most obvious routes of infectivity for a disease agent that is transmissible via oral exposure is through the lymphatic system and/or the circulatory system. While the lymphatic system has been theorized to be the primary route of infectivity for TSEs, the data supporting this theory are far from conclusive. Animal studies have demonstrated that TSEs, including BSE, can be transmitted via the blood through cut or abraded skin and damaged oral mucosal tissue. 6/ In addition, FDA has stated that "[t]he concentration of abnormal prion protein seen in vCJD lymphoid tissues has led to concerns that transmission of vCJD by blood might be a greater risk than for CJD." 7/ Furthermore, because there is great uncertainty surrounding the potential for TSEs to be transmissible via the blood – and even animal models that suggest that such transmission may be possible – FDA has recommended that blood donors who are at increased risk for developing vCJD due to potential exposure to the BSE agent should be deferred to prevent vCJD transmission by blood and blood products. 8/

### C. Request to Expand Scope of Prohibited Materials

As a result of the high degree of uncertainty surrounding the transmissibility of TSE agents through blood and blood products, combined with the fact that TSEs are *always* fatal, we believe FDA must broaden its scope of prohibited bovine-derived material to adequately protect the food supply – and the public health – in the U.S. from BSE. We contend that prohibiting bovine blood-derived products, such as beef blood plasma and fibrinogen, is not only a prudent

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5/ *Id.* at 42258.

6/ *Id.* at 42260.

7/ FDA, Guidance for Industry: Revised Preventive Measures to Reduce the Possible Risk of Transmission of Creutzfeldt-Jakob Disease (CJD) and Variant Creutzfeldt-Jakob Disease (vCJD) by Blood and Blood Products (January 2002), available at www.fda.gov/cber/gdlns/cjdvcjd.htm.

8/ *See id.*

step, but a necessary step, towards limiting consumers' exposure to food products with a high potential for transmitting the agent that causes vCJD. Only if and when the scientific knowledge about TSEs and its causative agents is more fully elucidated should the scope of prohibited bovine-derived material exclude any tissue that is acknowledged to have the potential to transmit these diseases.

For the reasons specified above, we respectfully submit that the list of prohibited bovine-derived material be expanded to include bovine-derived blood products.

Sincerely,

R. G. Bursey

Robert G. Bursey
Director, Regulatory Affairs
Ajinomoto Corporate Services, LLC